Treatment of Systemic Mastocytosis?

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Authors: Benjamin Liu, MD; MetroHealth, Internal Medicine; Saam Dilmaghani, MD; Mayo Clinic, Internal Medicine; Edited by: Matthew Hamilton, MD; Clinical Chief of Gastroenterology, Brigham Faulkner Hospital, Lead Gastroenterologist, Mastocytosis Center, Brigham and Women's Hospital, Assistant Professor of Medicine, Harvard Medical School

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What Is Systemic Mastocytosis?

Systemic Mastocytosis is a rare group of conditions where the body makes too many mast cells. Mast cells are a type of immune cell that help protect us from infections by releasing chemicals like histamine to generate an immune response. However, when there are too many mast cells, they can release these chemicals in large amounts. This usually results in symptoms like those found in allergic reactions. Some of these may be potentially life-threatening and known as anaphylactic reactions. Symptoms of anaphylaxis include swelling, hives, difficulty breathing, and feeling of passing out.

Hives – welts on the skin that are raised and itch.

How do we treat Systemic Mastocytosis?

The treatment for Systemic Mastocytosis depends largely on the subtype. There are several types of Systemic Mastocytosis. They differ in how many mast cells build up in the body, where they build up, and the type of symptoms and risk of complications. The following are the different subtypes:

- Indolent Systemic Mastocytosis (ISM)
- Smoldering Systemic Mastocytosis (SSM)
- Systemic Mastocytosis with an Associated Hematologic Neoplasm (SM-AHN)
- Aggressive Systemic Mastocytosis (ASM)
- Mast Cell Leukemia (MCL)

Learn more about the types of Systemic Mastocytosis with IFFGD Fact Sheet No. 904

Generally, ISM and SSM are considered "indolent" meaning that they do not advance over time to a more aggressive type with high risk of complications and death. In fact, life expectancy in these conditions is generally estimated in decades rather than just years, depending on your other medical conditions. The life expectancy for other subtypes – ASM and SM-AHN – on the other hand are measured more in months and years. MCL has the worst prognosis.

Epinephrine – also known as adrenaline, is a medication that is typically used to treat very serious allergic reactions

Regardless of the subtype, people with Systemic Mastocytosis are at risk for life threatening anaphylaxis where there is a sudden onset of difficulty breathing, severe GI symptoms, hives and/or (and most commonly) low blood pressure with a feeling of passing out. These episodes may be triggered by a bee sting or other exposures such as a medication, contrast agent used for a radiology test, or a food. A medication called epinephrine is prescribed and necessary for all patients for these emergency purposes. Usually, 2 injection pens are provided and their use will be reviewed with the prescriber. Understanding when and how to use epinephrine is critical for anyone with Systemic Mastocytosis. It is helpful to get a blood tryptase measurement within 2-6 hours (most often this is done in the Emergency Department) to confirm your flare was due to Systemic Mastocytosis. This information can be used to try to establish a trigger for the event and to potentially adjust the treatment plan.

One common trigger is having a medical procedure and surgery. To prevent the possibility of a flare, your providers should be made aware of your diagnosis of Systemic Mastocytosis before giving you any kind of anesthesia.

Non-Advanced disease (ISM and SSM)

Management for these subtypes is often focused on treating the symptoms of mast cell activation (flushing, itching, abdominal cramping, loose stools, throat tightness sensation). Additional treatments may be added to address more chronic symptoms such as fatigue and bone pain to improve quality of life. Finally, treatments may be needed for the complications of SM including bone loss and stomach ulcers.

Mast cell activation treatments include:

- **Antihistamines**: A drug or other compound that prevents the physiological effects of a compound (histamine) released by mast cells in response to injury or in allergic and inflammatory reactions. Some examples include cetirizine, fexofenadine, loratadine, hydroxyzine, and famotidine. Sometimes combinations of these are required, and diphenhydramine can be added for breakthrough symptoms (as needed).
- **Antileukotrienes**: After injury, infection, or contact with allergens your body produces a chemical called leukotrienes released by mast cells. Too much of this chemical can lead to a number of disorders with the most common being asthma and allergies. Antileukotrienes help regulate this chemical. Montelukast is an example, particularly if there is flushing, itching, or abdominal cramping that persists.
- **Cromolyn sodium**: A medication that is used as a mast cell stabilizer, meaning it prevents the release of inflammatory chemicals from the mast cells including histamine but many others as well. This is used more commonly for gastrointestinal symptoms.
- **Omalizumab and steroids**: these may be considered if there are recurrent episodes of emergency anaphylaxis requiring epinephrine.

Systemic Mastocytosis treatments to prevent complications may include:

- **Proton-pump inhibitors**: Medications that reduce stomach acid production such as omeprazole, esomeprazole, pantoprazole. These may be used if there are persistent symptoms of heartburn, acid reflux, and nausea and to heal ulcers if these are identified (by endoscopy)
- **Medications to prevent and treat bone loss**: Calcium and vitamin D supplementation is often needed to prevent bone loss and specific medications including the bisphosphonates may be prescribed once significant bone loss is detected. People with SM are often referred to a bone specialist.

If episodes of emergency anaphylaxis or mast cell activation symptoms persist despite current treatment, then it is best to speak to your healthcare provider for additional treatment options. Regardless, your physician will check blood work and other tests every 6-12 months to monitor disease progression, at which point treatment options would change.

In 2023, the Food and Drug Administration approved avapritinib (Ayvakit™) for adults with Indolent Systemic Mastocytosis (ISM). Avapritinib is in a class of medications called tyrosine kinase inhibitors. It works by blocking the action of the abnormal protein that signals mast cells to multiply. This daily medication is the only FDA approved medication for ISM. Prior, in 2023, it was approved for other types of Systemic Mastocytosis.

Advanced disease (ASM, MCL, SM-AHN)

As mentioned, the prognosis for advanced disease is measured more in months and years. The treatment for these subtypes of Systemic Mastocytosis can be complex and should be discussed with your healthcare providers and team. The approach varies depending on the specific subtype, and can include therapy to reduce cell counts, which can include types of chemotherapy or stem cell transplantation.

In 2021, the Food and Drug Administration approved avapritinib (Ayvakit™) for adult patients with Advanced Systemic Mastocytosis (AdvSM), including patients with Aggressive Systemic Mastocytosis (ASM), Systemic Mastocytosis with an Associated Hematological Neoplasm (SM-AHN), and Mast Cell Leukemia (MCL). Avapritinib is in a class of medications called tyrosine kinase inhibitors. It works by blocking the action of the abnormal protein that signals mast cells to multiply. It comes as a tablet to take by mouth. It is usually taken once daily on an empty stomach, at least 1 hour before and 2 hours after a meal.

Regardless of the treatment approach for advanced disease, clinicians will monitor blood work every 1-3 months. Additionally, it is common to repeat a bone marrow biopsy and get imaging at about 3 months after treatment to assess the response.

The Food and Drug Administration (FDA) is one of the U.S. government's regulatory agencies. This agency oversees a broad range of topics that pertain to food, drugs and other products used on a daily basis. The FDA works to protect public health by assuring that foods and drugs for humans and animals are safe and properly labeled. The FDA also ensures that vaccines, other biological products, and medical devices intended for human use are safe and effective. Products approved by the FDA have been deemed safe, with benefits that are worth the possible risks. This is done after reviewing studies and tests that have been done on a product.

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IFFGD
537 Long Point Road, Unit 101
Mt Pleasant, SC 29464